DISTRIBUTION OF 2,3,4,7,8-PENTACHLORODIBENZOFURAN (PeCDF) HALF-LIVES IN YUSHO PATIENTS

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1. Introduction

Yusho was a food poisoning incident that occurred in western Japan in 1968. Initial reports indicated that Yusho was caused by polychlorinated biphenyls. However, following a number of studies, it is now considered that Yusho was mainly caused by 2,3,4,7,8-pentachlorodibenzofuran (PeCDF) [1,2]. The concentrations of dioxins in the blood of Yusho patients have been measured at annual medical checkups[3,4].

We presented findings on the half-lives of PeCDF, which were inconsistent with those of other studies[5]. Many groups have reported half-lives of less than 10 or 15 years[6,7]. We identified two peaks: one was similar to that reported by other groups, but the other was a near-infinite half-life. In this study, we aimed to confirm the distribution of the half-lives of 2,3,4,7,8-PeCDF in Yusho patients. Our half-life calculations were more reliable than those of previous studies owing to the greater number of measurements for each patient and the increased period between the first and last measurements.

2. Materials and methods

The subjects were 395 patients whose blood concentrations of 2,3,4,7,8-PeCDF had been measured three or more times at annual Yusho medical checkups between 2002 and 2010 and for whom the period from the first to last measurement was over 3 years. One patient was excluded because the concentration dropped to one-third the original level in the 1st year, and it remained at that concentration throughout the study period. Table 1 shows the distribution of the patients by sex and age in 2006, which was the middle of the measurement period.

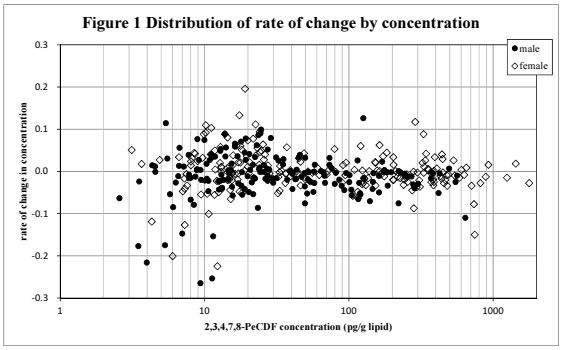
Table 1 Distribution by age an sex

age	male	female
20-30	4	0
30-40	16	13
40-50	18	22
50-60	29	36
60-70	43	62
70-80	56	63
80-90	20	12
90-100	0	1

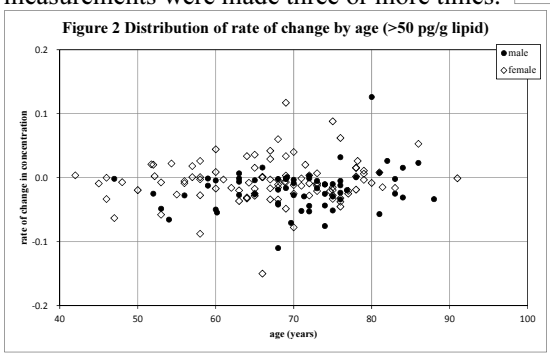
For each patient, linear regression analysis was performed with the logarithm of 2,3,4,7,8-PeCDF concentration in the blood lipid as the dependent variable and the year of measurement as the independent variable, using the following function:

$$lnC_{it} = k_i \cdot t + lnC_{i0}$$

The slope produced using the results of this equation indicated the rate of change in concentration. This rate of change in concentration was affected not only by excretion but also by ingestions, change in body weight, and measurement error. The rate of change in concentration was determined as being directly caused by the change in weight when the rate of change in concentration was calculated from two measurements for each patient. To reduce the effects of changes in weight and measurement errors, this study included only patients for whom the



measurements were made three or more times.



3. Results and discussion

Figure 1 is a scatter plot of the 2,3,4,7,8-PeCDF concentration and rates of change in concentration. Many patients with less than 30 pg/g lipid showed increasing concentrations; this was because the ingestion levels were comparable with the excretion level, and their concentrations were about at the level of that of the general public. Many patients with more than 30 pg/g lipid had a negative rate of change in concentrations, which signifies decreasing concentrations. Figure 2 is a scatter plot of the ages and rates of change in concentrations for patients with more than 50 pg/g lipid. About half the female patients showed a positive rate of change. Most male patients had negative rates of change. However, many male patients aged over 80 years presented a positive rate of change in concentration. Further, many female patients had a negative rate of change. It could be that a change occurs around the age of 80 years among males and 50 years among; however, there were too few patients in this study to confirm this.

Figure 3 shows the distribution of the half-lives by 2,3,4,7,8-PeCDF concentration ranges. Some patients showed near-infinite half-lives, and some patients had concentrations of over 50 pg/g lipid for less than 10 years. Patients with concentrations of 200–500 pg/g lipid had infinite half-lives. We identified one peak for infinite half-lives and another weak peak of 10–13.3 years for the patients whose concentration was 100–200 pg/g lipid. There was one peak of infinite half-lives for concentrations of 50–100 pg/g lipid.

For patients with 100–200 pg/g lipid, the half-lives in this study were largely at infinity or at the weaker peak of under 10 years. In our previous study, there were two peaks: one was near infinity, and the other was less than 10 years[5]. In this report, patients with concentrations of 100–200 pg/g lipid were mainly at near infinity and 10–13.3 years. The peak at about 10 years appeared to become lower, which resulted in longer half-lives than those found in our previous report.

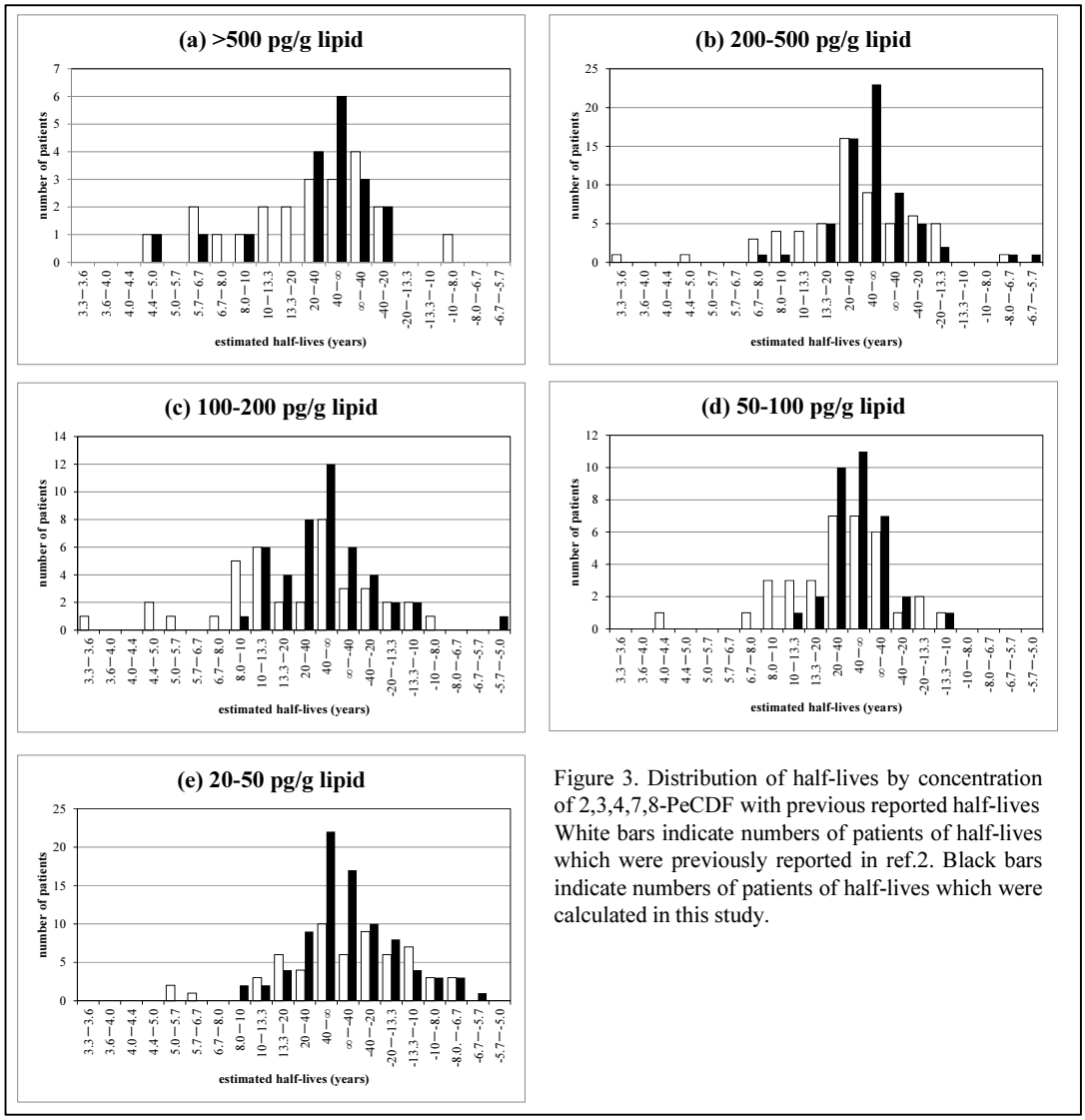


Figure 3. Distribution of half-lives by concentration of 2,3,4,7,8-PeCDF with previous reported half-lives White bars indicate numbers of patients of half-lives which were previously reported in ref.2. Black bars indicate numbers of patients of half-lives which were calculated in this study.

However, many groups have reported shorter half-lives of 10 or 15 years[6,7]. Thus, their results are inconsistent with our own. Our finding of two peaks and the inconsistency with the results of other studies could be due to the following: (1) rapid physiological changes, such as menopause, resulted in changes in the dioxin excretion rate; (2) the degree of obesity is a factor for physiological mechanisms in the excretion of dioxins. Menopause is a physiological event that occurs in women during their late 40s or early 50s, and it may therefore be related to the half-life of 2,3,4,7,8-PeCDF in female Yusho patients. As shown in Figure 2, the half-lives in female and male patients showed a marked shift at approximately 50 years and 80 years, respectively. The body

mass indexes (BMIs) in the present study were 23.7±2.5 (mean±SD) for males and 22.9±3.4 for females, which were lower than in the report by Aylward et al. [8]. They found BMIs to range from 32.0±4.3 (initial measurement) to 32.1±4.6 (second measurement), and the half-lives of dioxins from two measurements for each patient exposed in occupation with under 80 years. The differences in BMI may affect lipid excretion. Since we reported that lipid excretion from the skin can influence the excretion of dioxins[9], further investigation into the relationship between the difference in BMI and lipid excretion from the skin is required.

4. Acknowledgements
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